IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application Number	: 10/529,479	Confirmation No.:	TBA
Applicant	: Lasse L. HESSEL et al.		
Filed	: March 28, 2005		
Title	: A METHOD FOR DETECTING, SCREENING AND/OR MONITORING A CANCER IN AN INDIVIDUAL		
TC/Art Unit	TBA		
Examiner:	TBA		
Docket No.	: 59866.000004		
Customer No.	: **21967**		

SECOND PRELIMINARY AMENDMENT UNDER 37 C.F.R. §1.115

Attention Of: Mr. Leonard E. Smith
Mail Stop: PCT
Attn: Office of PCT Legal Administration
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Prior to examination on the merits, and further to a Preliminary Amendment Under 37 C.F.R. § 1.115, filed on March 28, 2005, please amend the above-identified patent application as follows:

Amendments to the Specification begin on page 2 of this paper.

Amendments to the Claims are reflected in the listing of claims which begins on page 4 of this paper.

Remarks begin on page 8 of this paper.

AMENDMENTS TO THE SPECIFICATION:

Please add the new paragraph on page 1, line 3, after the title, "A METHOD FOR DETECTING, SCREENING AND/OR MONITORING A CANCER IN AN INDIVIDUAL".

CROSS-REFERENCE TO RELATED APPLICATIONS

This patent application is a U.S. national phase application of PCT/DK/2003/000634, filed September 26, 2003, which claims priority to Denmark Patent Application No. 2002 01430, filed September 26, 2002, both of which are incorporated herein by reference in their entireties. This patent application is also a continuation-in-part of U.S. patent application 09/546,573, filed April 10, 2000 ("'573 application"), and a continuation-in-part of U.S. patent application 10/117,030, filed April 8, 2002 ("'030 application"). The '573 and '030 applications claim priority to Denmark Patent Application No. DK 1999 00476 filed April 9, 1999 ("DK '0476 application"). The entire contents of the '573, '030 and DK '0476 applications are incorporated herein by reference in their entireties.

Please delete the paragraph at page 8, before line 4, and insert the replacement paragraph as indicated below:

One embodiment of the invention is directed to a method for detecting a cancer in an individual, screening an individual for cancer, monitoring an individual for cancer, or the combination of the detecting, the screening and the monitoring an individual for cancer. The method comprises determining a first parameter represented by a concentration of TIMP-1 in at least one excreta from the individual. The presence of the first parameter above a predetermined discrimination value is an indication that the individual has a high likelihood ~~(such as a high likelihood)~~ of having the cancer or that there is a progression of the cancer in the individual.

Please delete the paragraph 3, at page 9, lines 14-17, and insert the replacement paragraph as indicated below:

Such cancers could comprise, e.g., breast, prostate, colorectal, cervical, ovarian, lung, pancreatic, renal, vulvar, hepatocellulæar carcinomas, minimal residual disease and recurrent cancer. ~~In this application whenever a group~~

~~of elements is recited with the transitional phrase "comprising", it is understood that we also contemplate the same group of elements with transitional phrases "consisting essentially of", "consisting", or with the phrase "selected from the group of consisting of" preceding the recitation of the elements. Thus, such cancers are, e.g., selected from the group consisting of breast carcinoma, prostate carcinoma, colorectal carcinoma, cervical carcinoma, ovarian carcinoma, lung carcinoma, pancreatic carcinoma, renal carcinoma, vulvar carcinoma, hepatocellulæar carcinoma, minimal residual disease and recurrent cancer, and, optionally, mixtures thereof.~~

AMENDMENTS TO THE CLAIMS:

Please amend claim 26 as follows.

1. (Original) A method for detecting and/or screening and/or monitoring a cancer in an individual, said method comprising determining a first parameter represented by the concentration of TIMP-1 in at least one excreta from the individual, wherein the presence of the first parameter above a predetermined discrimination value is an indication that the individual has a high likelihood of either having a cancer or progression in a cancer.

2. (Previously Presented) A method according to claim 1 wherein the cancer is selected from the group consisting of breast carcinoma, prostate carcinoma, colorectal carcinoma, cervical carcinoma, ovarian carcinoma, lung carcinoma, pancreatic carcinoma, renal carcinoma, vulvar carcinoma, hepatocellulæar carcinomas, minimal residual disease and recurrent cancer.

3. (Previously Presented) A method according to claim 1, wherein the excreta is saliva.

4. (Previously Presented) A method according to claim 1, wherein the first parameter is the total concentration of TIMP-1.

5. (Previously Presented) A method according to claim 1, wherein the first parameter is the combination of the concentration of total TIMP-1 and the concentration of free TIMP-1.

6. (Original) A method according to claim 5, wherein the combination is performed by logistic regression analysis.

7. (Previously Presented) A method according to claim 1, wherein the discrimination value is determined by determining the total concentration of TIMP-1 in the at least one excreta in both a healthy control population and a population with

known cancer, thereby determining the discrimination value which identifies the cancer population with a predetermined specificity or a predetermined sensitivity.

8. (Previously Presented) A method according to claim 1, wherein the method further comprises determining at least one second parameter representing the concentration of a marker for cancer different from any form of TIMP-1, in an excreta from an individual.

9. (Previously Presented) A method according to claim 8, wherein the first and second parameter are combined to result in a combined parameter wherein the presence of a concentration of the combined parameter above a predetermined discrimination value is an indication that the individual has a high likelihood of having a cancer or that there is a progression in a cancer.

10. (Previously Presented) A method according to claim 9, wherein the predetermined discrimination value is determined by determining the combined parameter in the at least one excreta in both a healthy control population and a population with known colorectal cancer, thereby determining the predetermined discrimination value which identifies the cancer population with a predetermined specificity or a predetermined sensitivity.

11. (Previously Presented) A method according to claim 9, wherein the combination of the first and second parameter is performed by logistic regression analysis.

12. (Previously Presented) A method according to claim 8, wherein the at least one second parameter is the concentration of Carcino Embryonic Antigen (CEA).

13. (Previously Presented) A method according to claim 7, wherein the determination of the total concentration of TIMP-1 is performed by means of an immunoassay or an active assay.

14. (Previously Presented) A method according to claim 13, wherein the immunoassay is an ELISA.

15. (Previously Presented) A method according to claim 13, wherein the active assay is zymography.

16. (Previously Presented) A method according to claim 1 which detects early stage cancer.

17. (Previously Presented) A method according to claim 16, which detects early stage colorectal cancer.

18. (Previously Presented) A method according to claim 16, which detects metastatic breast cancer.

19. (Previously Presented) A method according to claim 1, which monitors the response to cancer treatment.

20. (Previously Amended) A method according to claim 1, which monitors the recurrence of a cancer.

21. (Previously Presented) A dipstick for performing the method according to claim 1, wherein said dipstick comprises a first colour indication zone, comprising antibodies specific for TIMP-1.

22. (Previously Presented) A dipstick according to claim 21, wherein the first zone further comprises at least one reagent which gives an optically visible colour change in the zone dependent on the concentration of TIMP-1 in at least one excreta.

23. (Previously Presented) A dipstick according to claim 21, wherein the dipstick further comprises a second colour indication zone, able to react with at least

one substance normally present in the excreta, and thereby providing an optically visible colour change in the zone for controlling proper use of the dipstick properly.

24. (Previously Presented) A dipstick according to claim 23, wherein said dipstick further comprises a third colour indication zone, comprising antibodies specific for CEA.

25. (Previously Presented) A dipstick according to claim ~~21~~-24, wherein the first zone further comprises at least one reagent which can give an optically visible colour change in the zone dependent on the concentration of CEA in at least one excreta.

26. (Currently Amended) A method according to claim 1 wherein the cancer comprises breast carcinoma, prostate carcinoma, colorectal carcinoma, cervical carcinoma, ovarian carcinoma, lung carcinoma, pancreatic carcinoma, renal carcinoma, vulvar carcinoma, hepatocellulæar carcinoma, minimal residual disease ~~or~~ and recurrent cancer.

REMARKS

Claim 26 amendments are supported by the specification, including original claims, considered as a whole e.g., claim 2.

An indication of allowance of all claims is respectfully requested.

Authorization is hereby granted to charge or credit the undersigned's Deposit Account No. 50-0206 for any fees or overpayments related to the entry of this Amendment.

Respectfully submitted,

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